(NO. 5573). All the SEQ ID NOs were inserted after the sequence that they identify. No new matter has been included by this amendment.

The paragraph on page 16, lines 1-8, of the specification was amended to provide clarification and to include the appropriate SEQ ID NO, in compliance with 37 C.F.R. § 1.821-1.825. Specifically, 5' and 3' were added to the ends of the exemplary core sequences so as to provide orientation. In addition, on line 8, after "GCCGUUAGGC" was added "SEQ ID NO 5574".

The tables III-VII (pages 53-129 as originally filed) of the specification were amended to remove any redundant sequences, and provide unique SEQ ID NOs for the sequences included therein, in compliance with 37 C.F.R § 1.821-1.825. The Tables, as originally filed, did not identify the sequences by SEQ ID NOs. Additionally, the ribozyme sequences in tables III and IV have been amended, replacing "X" with the sequence "GCCGUUAGGC". Support for the replacement of "X" with "GCCGUUAGGC" can be found at the end of the originally filed Tables III and IV (pages 61 and 84). Lastly, the "target sequences" found in Tables III, IV, and VI were originally disclosed with the nucleotide "T" instead of "U". As the target sequences are RNA sequences, the "T" nucleotides have been amended to "U." One of skill in the art would be able to recognize that the ribonucleotide "U" corresponds to the deoxyribonucleotide "T".

These amendments do not constitute new matter, and only serve to clarify the invention. Accordingly, no new matter has been added by way of any of these amendments to the specification.

New tables III-VII are found on substitute sheets 53-129, submitted herewith.

A copy of the marked up original paragraphs of the specification showing changes made by these amendments is attached as **APPENDIX A**.

Abstract

Substitute page 133 contains the amended abstract, which has been amended by insertion of the phrase "The present invention relates to" at the beginning of the sentence.

The abstract was amended to provide clarification of the subject matter of the invention

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and to correct grammatical errors. Accordingly, no new matter has been added by way of the amendments. A copy of the marked up original abstract is attached as **APPENDIX B**.

Figures

Figures 1-4 have been amended to include the appropriate SEQ ID NOs in compliance with 37 C.F.R § 1.821-1.825. In addition, some format changes have been made merely to clarify the subject matter of the Figure, including using solid font for "C" and "U" in Figures 3 and 4 and "U_4" in Figure 2. The title of Figure 4 has been modified in order to more accurately describe its contents. No new matter has been added by way of these amendments. A marked up copy of the changes made to the original Figures is attached as **APPENDIX C**.

Sequence Listing

Applicant submits herewith a sequence listing that corresponds with the SEQ ID NOs in the substitute tables III-VII, submitted herewith. In addition, the new sequence listing includes the sequences found in the specification and Figures.

In compliance with 37 C.F.R § 1.821-1.825 and § 1.52(e), the applicant herewith submits the Sequence Listing on Compact Disc-Recordable (CD-R) medium in duplicate (COPY 1 and COPY 2), in lieu of the paper copy under 37 C.F.R. § 1.821(c), and computer readable form copy (COPY 3). The paper and computer readable forms of the Sequence Listing are the same. The Statement under 37 CFR § 1.821(f) is also provided.

The Sequence Listing has been generated from the specification and does not constitute new subject matter. The Sequence Listing has been prepared in the PatentIn Ver.3.0 format and checked with Checker Version 3.0 Program. No error has been found.

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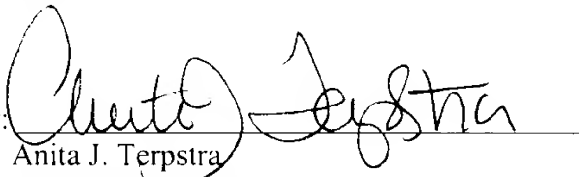
The Commissioner is hereby authorized to charge payment of any fees required in connection with the papers transmitted herewith, or to credit any overpayment of same, to Deposit Account No. 13-2490. If the Examiner has any questions regarding this Preliminary Amendment, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

McDonnell Boehnen Hulbert & Berghoff

Date: September 13, 2001

By: 
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APPENDIX A
Version With Markings to Show Changes Made to Specification

Bold, underline text, **for example**, indicates inserted text
Bracketed, strikethrough text, [~~for example~~], indicates deleted text

IN THE SPECIFICATION:

The paragraph on page 8, line 22 – page 9, line 17:

Telomerase may be assayed according to Kim and Wu, *Nucl. Acids Res.* 25: 2595-2597, incorporated herein by reference. Briefly, for the telomerase assay, 2µg of protein extract is used. The extract is assayed in 50µl of reaction mixture containing 0.1 µg TS substrate primer (5'-AATCCGTCGAGCAGAGTT-3' **(SEQ ID NO 5569)** end-labeled using alpha-^{32}P-ATP and T4 polynucleotide kinase) **(SEQ ID NO 5570)** 0.1µg ACX return primer (5'-GCGCGG[CTTACC]$_3$ CTAACC-3'), 0.1 µg NT internal control primer (5'-ATCGCTTCTCGGCCTTTT-3') **(SEQ ID NO 5571)** 0.01 micromol TSNT internal control template (5'-AATCCGTCGAGCAGAGTTAAAAGGCCGAGAACGAT-3') **(SEQ ID NO 5572)** 50 µM each deoxynucleoside triphosphate, 2 U of Taq DNA polymerase, and 2 µl CHAPS protein extract, all in 1X TRAP buffer (20 mM Tris (pH 8.3), 68 mM KCl, 1.5 mM $MgCl_2$, 1 mM EGTA, 0.05% Tween 20). Each reaction is placed in a thermocycler block preheated to 30 C and incubated at 30 C for 10 minutes, then cycled for 27 cycles of 94 degrees C for 30 seconds, 60 degrees C for 30 seconds. Reaction products are separated on a denaturing 8% polyacrylamide gel, followed by drying of the gel and autoradiography. The internal control (to control for possible Taq polymerase inhibition) generates a band of 36 nt. Comparison of radioactive signal integrated (*e.g.*, by phorphorimager analysis) for telomerase-extended bands with the radioactive signal from a reaction performed with a known amount of quantification standard template (termed R8; 5'-AATCCGTCGAGCAGAGTTAG [GGTTAG]$_7$-3') **(SEQ ID NO 5573)** allows expression of telomerase activity as an absolute value. The absolute value = TPG (total product generated) =[(TP-TPi)/TI]/[(R8-B)/RI)] x 100, where TP = telomerase products from test extract, TPi = telomerase products from a heat-inactivated (75 C, 10 minutes) extract reaction, TI = the signal from the internal control, R8 = the signal from the R8 qualification standard template reaction, B = signal from a lysis buffer-only blank reaction, and RI = the internal control value for the reaction containing R8 template and NT and TSNT control primers. TPG values of 0-10,000 are possible, with the linear range being from approximately 1 to 1000 TPG. The range of 1 to 1000 TPG encompasses the minimum and maximum levels of telomerase activity in most tumor samples tested, while non-tumor cells most often have no telomerase activity (TPG approximately zero).

The paragraph on page 16, lines 1-8:

By "consists essentially of" is meant that the active ribozyme contains an enzymatic center or core equivalent to those in the examples, and binding arms able to bind mRNA such

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that cleavage at the target site occurs. Other sequences may be present which do not interfere with such cleavage. Thus, a core region may, for example, include one or more loop or stem-loop structure[s], which do**es** not prevent enzymatic activity. **The underlined regions** [~~"X"~~] in the sequences in **Tables III** and **IV** can be such a loop**, and can be represented generally as sequence "X"**. **For example, a** [~~A~~]core sequence for a hammerhead ribozyme can be **5'-**CUGAUGAG**-3' and** [~~X~~]**5'-**CGAA**-3' connected by "X",** where X[=] **is 5'-**GCCGUUAGGC**-3' (SEQ ID NO 5574),** or other stem II region known in the art.

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APPENDIX B
Version With Markings to Show Changes Made to Abstract

Bold, underline text, **for example**, indicates inserted text
Bracketed, strikethrough text, [~~for example~~], indicates deleted text

IN THE ABSTRACT:

The present invention relates to [~~N~~]nucleic acid molecules which modulate[~~s~~] the synthesis, expression and/or stability of an RNA encoding one or more protein subunit of telomerase enzyme.

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Notice to Comply	Application No. 09/653,225	Applicant(s) Chowrira et al
	Examiner T. Larson	Art Unit 1635

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: SEQ. ID. NOS. are missing from disclosure.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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